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(A,B,C) and 56 different class II (DR,DQ,DP) alleles on a Luminex platform (One Lambda, Canoga Park, CA) to determine antibody production in both the GVH and HVG directions. Since the threshold Ab response to HLA MM in marrow transplantation is unknown, we applied the established scale from solid organ transplantation where ≥1000 is positive, 500–999 is possible, and <500 is negative. The limitation of the analysis is that the beads contain every antigen but not every allele. In the 40 pairs, no anti-A, B, or C allele-specific antibodies were detected at day 100 in either direction. Results for class II antibody are shown in the table below. There is evidence for class II allele-specific antibody production to the MM allele in both the GVH and HVG directions with the highest frequency Ab seen against DPA1. In conclusion, day 100 Ab to class II rather than class I allele MM are observed in this pilot study. This may reflect greater immunogenicity of class II as compared to class I, a longstanding observation in transplantation. Current studies to determine if these are de novo or preformed Ab are being performed using pretransplant sera from these same pairs. Future studies will look at Ab association with GVHD and disease relapse with attention to class II on B cells as a meaningful GVL target.

Class II Antibody Analysis

	DRB1	DQB1	DQA1	DPB1	DPA1
# of GVH disparate alleles	8	13	8	46	14
Allele Ab test available	3	7	5	13	11
Frequency of Ab≥ 1000	0	0	0	2/13 (15%)	2/11 (18%)
Frequency of Ab≥500	2/3 (67%)	2/7 (29%)	0	4/13 (31%)	6/11 (55%)
# of HVG disparate alleles	8	13	9	44	13
Allele Ab test available	1	2	6	17	10
Frequency of Ab≥1000	0	0	0	0	2/10 (20%)
Frequency of Ab≥500	1/1 (100%)	0	0	5/17 (29%)	7/10 (70%)

GVH=graft-versus-host; HVG=host-versus-graft.

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IS THERE REALLY A DIFFERENCE IN OUTCOME AND INCIDENCE OF ACUTE/CHRONIC GVHD IN PATIENTS UNDERGOING UNMANIPULATED MUD-PBSCT VS MUD-BMT? SINGLE LARGE PEDIATRIC CENTER EXPERIENCE

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There is an unresolved question whether unmanipulated matched unrelated donor (MUD) PBSCT leads to a worse overall outcome and higher incidence of severe GvHD in comparison with well established MUD-BMT. It is well known that PBSC grafts contain ca 1 log more mature T cells, which may result in higher rate of severe and often fatal acute/chronic GvHD after MUD-PBSCT. The aim of our study was to compare the results of MUD-PBSCT vs MUD-BMT in a large mostly pediatric patient population. We analyzed the records of 177 consecutive pts (with hematologic malignancies, n = 148 and non-malignant disorders, n = 29), who underwent MUD-BMT (42 pts) or MUD-PBSCT (135 pts) between 1999 and February 2008 in our department. Probability of overall survival for all pts after MUD-PBSCT was 0.54 and after MUD-BMT was 0.46 (p = NS). Median follow-up of surviving 97 pts (55%) was 3 years. Furthermore, there was no difference between the probability of incidence of both acute GvHD grade III-IV between the recipients of MUD-PBSCT (0.2) or MUD-BMT (0.25) and extensive chronic GvHD (0.21 for MUD-PBSCT recipients and 0.18 for MUD-BMT recipients). With regard to "high resolution" HLA match, 84 donor-recipient pairs were fully matched, whereas 64 were mismatched at one, 24 at two and 5 at three loci. Probability of survival, acute GvHD grades III-IV and extensive cGvHD were for respective groups as follows: 0.53, 0.18, 0.17 for 10 of 10 allele matched group, 0.47, 0.21, 0.18 for 9 of 10 allele matched group and surprisingly 0.58, 0.27 and 0.27 for 8 of 10 allele matched group. In the latter group, however, if two HLA antigens were mismatched the probability of survival decreased to 0.38, probability of severe aGvHD increased to 0.46 and of extensive cGvHD to 0.6. If only one antigen + one allele or two alleles were mismatched, the probability of survival was as high as 0.65 and probability of severe aGvHD as low as 0.19. In conclusion, the results of MUD-PBSCT in a large prospective cohort of pts are similar if not better than the results of MUD-BMT. There seems to be no increased risk of severe GvHD after MUD-PBSCT. MUD-PBSCT might offer a better disease control in patients with malignancies, especially with AML. With regard to the degree of HLA match it seems that transplants from 8 of 10 allele matched donors (with maximum 1 mismatched antigen) influence neither survival nor incidence of severe GvHD, whereas one should avoid performing transplants from two antigen mismatched donors.

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REDUCED-INTENSITY CORD BLOOD TRANSPLANTATION FOR ADULT PATIENTS WITH ACUTE MYELOID LEUKEMIA/MYELODYSPLASTIC SYNDROME

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Objectives: To investigate relevant factors affecting the outcome of reduced-intensity cord blood transplantation (RI-CBT), we analyzed retrospectively the results of 128 adult patients with acute myeloid leukemia (AML)/ myelodysplastic syndrome (MDS) in Toranomon hospital.

Patients and Methods: We reviewed medical records of 128 patients with AML/MDS who had received RI-CBT between Feburuary 2002 and July 2007 at Toranomon Hospital, Tokyo, Japan. The following factors were considered as potential predictors of outcomes: patient's age, ECOG performance status (PS), HLA disparity, infused Total nucleated cell (TNC) dose/CD34 dose, disease/disease status, cytogenetics (SWOG/ECOG criteria) at UCBT, acute graft versus host disease (GvHD) and chronic GvHD. All factors were tested for the proportional hazards assumption. Time to event curves were plotted by using the actuarial method of Kaplan-Meier and differences between curves were analyzed by log-rank tests.

Results: Patient's median age was 58 years (17–82). Diagnoses include de novo AML (n = 68), MDS overt AML (n = 35), refractory anemia (RA) (n = 10), and refractory anemia with excess of blasts (RAEB) (n = 14). Eighty patients, who were at PS 0 or 1, and 47 patients were PS 2 or more. Disease status consisted of standard (n = 17) and advanced (n = 110). HLA disparities were 4/6 match (n = 83), 5/6 (n = 39), and 6/6 (n = 5). TNC/CD34 cell dose were 2.5×10E7/kg (1.8–4.5) and 0.7×10E5/kg (0.1 – 2.0), respectively. Main conditioning regimen was Fludarabine (125mg/m2) +Melphalan (80mg/m2) +TBI 4Gy. GvHD prophylaxis consisted of tacrolimus (Tac) alone in 68, Tac plus mycophenolate mofetil in 24, and cyclosporine alone in 35. All patient received single cord blood unit. Neutrophil engraftment was achieved in 86% (median 21 days). Incidence of grade **II-IV** acute GvHD and chronic GvHD were 40 and 22%, respectively. Transplantation -related mortality (TRM) at 2-years was 48% (95% CI 37–58). Estimated 3-years Leukemia free survival (LFS) was 25% (95% CI 16–36) and (standard risk 64% (95% CI 48–87) and high risk 17% (95% CI 6–27)). In univariate analysis, variables associated with improved survival were standard risk (P = 0.02) and PS 0–1 (p < 0.001), while other factors were not significant.

Discussion/Conclusion: We conclude that RI-CBT is a viable therapeutic option for adult AML/MDS patients. Higher TRM was the biggest problem to be solved to increase the feasibility of this approach.